Dynamics of particles with "key-lock" interactions

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The dynamics of particles interacting by key-lock binding of attached biomolecules are studied theoretically. Examples of such systems include DNA-functionalized colloids as well as nanoparticles grafted with antibodies to cell membrane proteins. Depending on the coverage of the functional groups, we predict two distinct regimes separated by a *percolation transition*. In the *localized regime* at low coverage, the system exhibits a broad, power law like distribution of particle departure times. At higher coverage, there is an interplay between departure dynamics and particle diffusion. This interplay leads to a sharp increase of the departure times, a phenomenon qualitatively similar to *aging* in glassy systems. This *diffusive regime* is analogous to dispersive transport in disordered semiconductors: depending on the interaction parameters, the diffusion behavior ranges from standard diffusion to anomalous, *subdiffusive* behavior. The connection to recent experiments and implications for future studies are discussed.

Selective key-lock interactions are quintessential for biology. Over the past several years, they have also attracted substantial attention in the context of nanoscience. It is becoming common practice to attach biomolecules capable of key-lock binding to colloidal particles or other microscopic objects to achieve controllable, specific interactions. Examples include nanoparticles functionalized with complementary single-stranded DNA (ssDNA) ([1]-[8]), or with antibodies to a particular protein. The possible applications range from self-assembly of smart nanomaterials to biosensors and cell-specific drug delivery ([9]-[11]). In this new class of systems, the collective character of the binding may lead to non-trivial and often prohibitively slow dynamics.

In this letter we report several remarkable results dealing with the dynamics of particles with reversible key-lock interactions. These results are of both conceptual and practical interest. In particular, we will demonstrate that depending on the coverage of the functional groups (e.g. ssDNA or proteins), the system exhibits two distinct regimes separated by a *percolation transition*. At low coverage, there is a broad power law like distribution of departure times but no lateral diffusion. If the coverage is sufficiently high, the overall particle dynamics is a result of the interplay between diffusion and desorption. The lateral motion is analogous to *dispersive transport* in disordered semiconductors: it may range from regular diffusion with a renormalized diffusion coefficient, to anomalous, subdiffusive behavior.

In the simplest version of our model, a single particle interacts with a flat $2D$ surface via multiple key-lock binding (see Figure 1). At each position of the particle, there are m key-lock bridges which may be closed or open, and there is a binding energy ϵ for each of the key-lock pairs (the variation in ϵ is neglected). Therefore, the m-bridge free energy plays the role of an effective local potential for the particle: $U(m) = -k_B T m \Delta$, where $\Delta \equiv \log\left(1 + \exp\left[\epsilon/k_B T\right]\right)$ [12]. In a generic case, the number of bridges m is a Poisson distributed random number $P_m = \overline{m}^m \exp\left(-\overline{m}\right)/m!$ where $\overline{m}$ denotes the mean of the distribution. After staying for some time at a particular site, the particle either breaks all its bridges and departs, or hops a distance a to a new site characterized by a new value for the number of bridges m. In this sense we have coarse-grained the particle motion by discrete steps of the correlation length a, the distance after which the number of bridges becomes statistically independent of the value at the previous location.

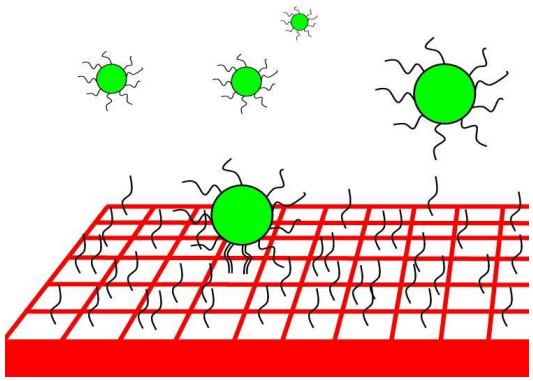

FIG. 1: (Color online). A snapshot of particles interacting with a two-dimensional substrate. Particles are alternately bound to the substrate by bridges, or unbound and free to diffuse in a direction normal to the substrate plane.

There is a percolation transition which separates the diffusive regime from the localized regime. In the localized regime the particle remains close to the original location until breaking all its bridges and departing. In the diffusive regime the particle undergoes a random walk by breaking and reforming multiple bridges. The transition between the two regimes occurs at the percolation threshold where one first encounters an infinitely connected cluster of sites with $m > 0$. Since the critical probability of bond percolation on the square lattice[13] is $\frac{1}{2}$, the transition is given by $P_0 = \frac{1}{2}$. Below, we cal-

culate the departure time distribution $\Phi(t)$ in both the localized and diffusive regimes, and study the random walk statistics above the percolation threshold.

Localized regime. Consider a particle attached to the substrate by m bridges below the percolation threshold $\overline{m} = \log 2$. The probability that the particle departs from the surface between time t and $t + dt$ is $\Phi_m(t)dt \simeq K_m \exp[-K_m t]\, dt$. The departure rate $K_m = \frac{1}{\tau_0}\exp(-\Delta m)$ is given by the Arrhenius relation $K_m \sim \exp\left(\frac{U(m)}{k_B T}\right)$ with τ_0 a characteristic timescale for bridge formation. By averaging this distribution over the statistics of m we arrive at:

$$\Phi(t) = \sum_{m=1}^{\infty} \exp[-K_m t]\, K_m \widetilde{P}_m \tag{1}$$

When performing the averaging we do not include states with $m = 0$ bridges. For this reason we work with a renormalized probability distribution $\widetilde{P}_m = P_m/(1 - \exp(-\overline{m}))$ so that $\sum_{m=1}^{\infty} \widetilde{P}_m = 1$.

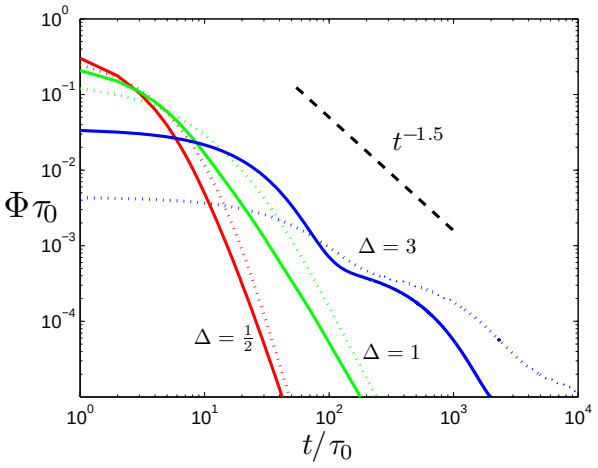

FIG. 2: (Color online). Departure time distribution function vs. time at the percolation threshold $\overline{m} = \log 2$. The solid lines are calculated from Eq. 1 in the localized regime, and the dotted curves are calculated from Eq. 4 in the diffusive regime.

The results of this calculation can be compared to a recent experiment which determined the time-varying separation of two DNA-grafted particles in an optical trap [1]. In this experiment two particles are bound by DNA bridges, and after breaking the connections diffuse to the width of the optical trap. Because the length of the DNA chains grafted on the particle is much less than the particle radius, surface curvature effects can be neglected. Hence, the experiment resembles a particle interacting with a localized site on a $2D$ substrate. Experimentally, the tail of the departure time distribution was observed to be a power law $\Phi(t) \sim t^{-1.5}$. Such behavior is indeed reproduced by Eq. 1 with a binding free energy on the order of several $k_B T$. For strong enough binding, $\Delta \gtrsim 1$, the departure time distribution function exhibits a pronounced multi-exponential character.

Diffusive regime. The departure time distribution is strongly altered above the percolation threshold. In this regime the particle can move around to find a more favorable state on the surface. This leads to a much longer lifetime of the bound state, a phenomenon similar to *aging* in glassy systems. The hopping rate between two neighboring sites is given by the Arrhenius law, $\kappa_{i\to j} \sim \frac{1}{\tau_0}\exp[-\Delta(m_i - m_j)\theta(m_i - m_j)]$. Here $\theta(x)$ is the Heaviside step function. The problem can be greatly simplified since the ensemble averaged hopping rate from a site with m bridges can be well approximated by an effective Arrhenius relation:

$$\kappa_m = \frac{1}{\tau_0}\exp[-\Delta(m - \overline{m})] \tag{2}$$

In the case when $\Delta\overline{m}$ is sufficiently large, the probability of staying attached to the surface after an n step random walk is $\left(1 - \frac{K_m}{\kappa_m}\right)^{n-1} = [1 - \exp(-\Delta\overline{m})]^{n-1}$. Interestingly, this probability is virtually independent of the particular bridge numbers $\{m_1, ..., m_n\}$ realized during the walk. We conclude that the probability of particle departure after exactly n steps is $f_n = [\exp(\gamma) - 1]\exp(-\gamma n)$, where $\gamma = -\log[1 - \exp(-\Delta\overline{m})]$. If we let $\phi_n(t)$ denote the departure time distribution for a walk of n steps we have:

$$\Phi(t) = \sum_{n=1}^{\infty} f_n \phi_n(t) = \sum_{n=1}^{\infty} f_n \prod_{i=1}^{n} \sum_{m_i=1}^{\infty} \widetilde{P}_{m_i}\kappa_{m_i} \times \int_0^{\infty} dt_i \exp(-\kappa_{m_i} t_i)\, \delta\left(t - \sum_{j=1}^{n} t_j\right) \tag{3}$$

To complete the calculation it is convenient to Fourier transform $\phi_n(t)$. One can then sum the resulting geometric series to obtain $\Phi(\omega)$ and perform the inverse transform to derive the following result:

$$\Phi(t) = \exp(\gamma)[\exp(\gamma) - 1] \sum_{r=1}^{\infty} \frac{\exp(-z_r t)}{Y(z_r)} \tag{4}$$

$$Y(z_r) = \sum_{m=1}^{\infty} \frac{\widetilde{P}_m \kappa_m}{(\kappa_m - z_r)^2} \tag{5}$$

Here z_r labels the roots of the equation

$$\exp(\gamma) - \sum_{m=1}^{\infty} \frac{\widetilde{P}_m \kappa_m}{\kappa_m - z} = 0. \tag{6}$$

In Figure 2 the two results for the departure time distribution are compared at the percolation threshold $\overline{m} = \log 2$. For fixed $\overline{m}$ a change in Δ is directly related to a change in the average binding free energy. As

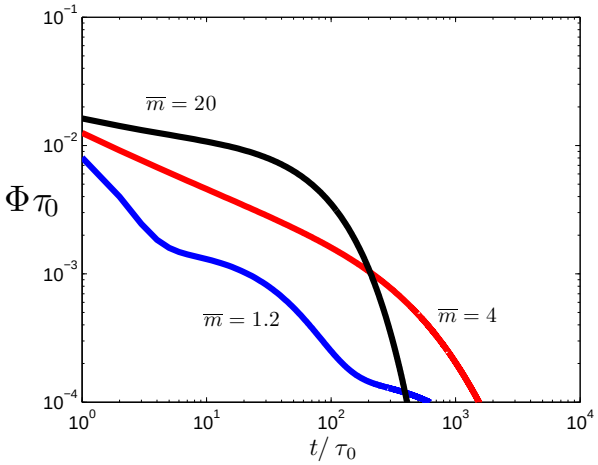

FIG. 3: (Color online). Departure time distribution function vs. time as determined by Eq. 4 in the diffusive regime. In the plot $\Delta\overline{m}=4$.

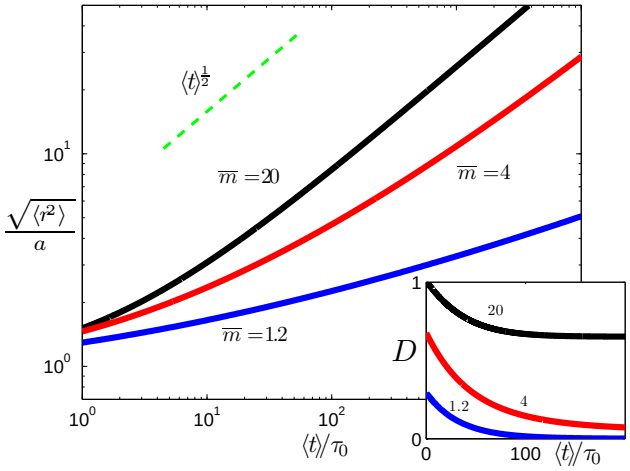

FIG. 4: (Color online). Rms displacement vs. time holding $\Delta\overline{m}=4$. The inset is the dimensionless diffusion coefficient defined as $D=\frac{1}{4D_0}\frac{\partial\langle r^2\rangle}{\partial\langle t\rangle}$ plotted against time.

indicated in the plot, increasing Δ decreases the rate of particle departure.

In Figure 3 we plot the departure time distribution as determined by Eq. 4 in the diffusive regime. In the figure we hold the product $\Delta\overline{m}=4$ constant. The optimal regime for fast departure is to have a large number of weakly bound bridges. In this case the departure time is well approximated as a single exponential, $\Phi(t)=K_{\overline{m}}\exp(-K_{\overline{m}}t)$.

Finally, we discuss the statistics of the in-plane diffusion of the particle. We notice that the in-plane *trajectory* of the particle subjected to a delta-correlated random potential remains statistically equivalent to an unbiased random work. Therefore, the mean-squared displacement after n steps is given by $\langle r^2\rangle=na^2$. However, as the particle explores the landscape the average hopping time becomes longer and the diffusion gets slower. In the limit $n\to\infty$, the average hopping time can be determined from the equilibrium canonical distribution. For the case of Poisson distributed m, this corresponds to a finite yet renormalized diffusion coefficient D^* with $D_0=a^2/4\tau_0$:

$$D^*\equiv\frac{1}{4}\frac{\partial\langle r^2\rangle}{\partial\langle t\rangle}=D_0\frac{\exp\left(\overline{m}e^{\Delta}\right)-1}{\exp\left(\Delta\overline{m}\right)\left[\exp\left(\overline{m}\right)-1\right]} \qquad (7)$$

However, it may take a very long time to achieve this "ergodic" behavior. In the transient regime, an $n-$step random walk cannot typically visit sites with an arbitrarily large number of bridges m. Instead, one should average the hopping times only over sites with $m<m^*$. In the language of the statistics of extreme events, m^*-1 is the maximum "expected" value of m in a sample of n independent events [14]. Both the average diffusion time $\langle t\rangle$, and mean square displacement $\langle r^2\rangle=na^2$, can be expressed in terms of m^*, which defines their relationship in parametric form:

$$\langle r^2\rangle=\frac{a^2}{P(\overline{m},m^*)} \qquad (8)$$

$$\langle t\rangle=\frac{\langle r^2\rangle}{D^*}\left(1-\frac{P(\overline{m}e^{\Delta},m^*)}{1-\exp\left(-\overline{m}e^{\Delta}\right)}\right) \qquad (9)$$

Here $P(x,m^*)\equiv\gamma(x,m^*)/\Gamma\left(m^*\right)=\exp\left(-x\right)\sum_{k=m^*}^{\infty}x^k/k!$ is the regularized lower incomplete Γ function. It is easy to see that in the limit $m^*\to\infty$ we recover the renormalized diffusion relation $\langle t\rangle=\langle r^2\rangle/D^*$, although this occurs at very long, often unrealistic times. In the transient regime we expect anomalous, subdiffusive behavior. As shown in Figure 4, this regime is typical for strong enough key-lock interactions. The predicted anomalous diffusion may be well described by a power law, $\langle r^2(t)\rangle\sim\langle t\rangle^{\alpha}$, with a non-universal exponent $\alpha<1$.

This work provides additional insight into the slow crystallization dynamics of key-locking particles (see figure 5). In [2], 1 μm diameter particles were grafted with ssDNA and formed reversible, disordered aggregates. The average number of key-lock bridges between particle pairs was $\overline{m}\sim1$. By further reducing the grafting density of DNA strands on the particles ($\overline{m}<1$), the authors of reference [1] observed random hexagonal close-packed crystals. Crystallization requires that colloids repeatedly depart and reattach to the growing structure, in an effort to find their desired lattice location. We can attempt to quantify this optimal experimental regime of fast departure by determining the time T required for

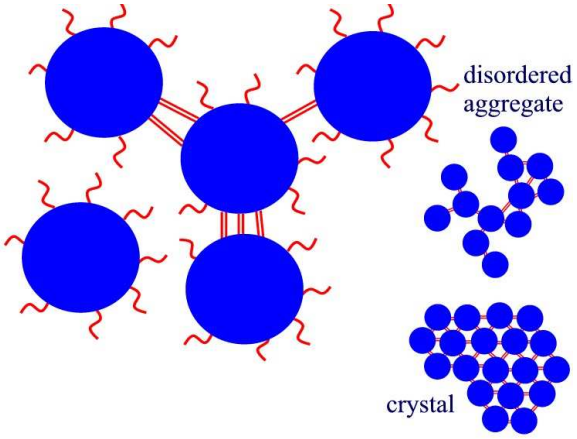

FIG. 5: (Color online). Schematic depiction of key-lock binding between nanoparticles functionalized with complementary ssDNA. The resulting structures can be disordered, fractal-like aggregates, or crystalline.

90% of the particles to depart: $0.1 = \int_T^\infty \Phi(t)dt$. Figure 6 is a plot of T vs. $\overline{m}$ at constant binding free energy [12]: $\frac{\Delta\overline{m}}{1-\exp(-\overline{m})} + \log(1-\exp(-\overline{m})) = const.$ The optimal regime is to have a large number ($\overline{m} \sim 10$) of weakly bound bridges. To realize this regime experimentally we propose the introduction of long, flexible DNA linkers to a system of particles with a high coverage of short ssDNA. This scheme increases the number of key-lock bridges between particle pairs as compared to previous experiments, and therefore has the potential to substantially reduce the time required for crystallization. The prediction of a localized regime below the percolation threshold (the local minima in Figure 6) where particle departure is relatively fast is confirmed experimentally by the crystallization observed in [1].

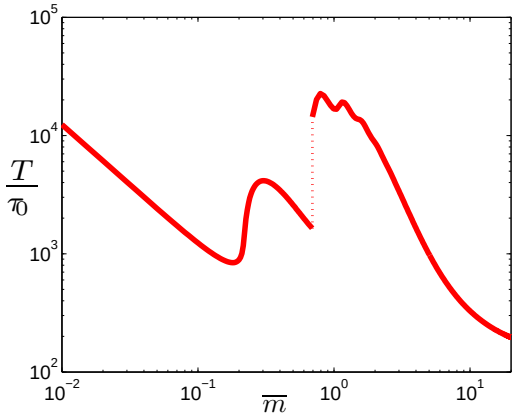

FIG. 6: (Color online). Plot of the time T required for 90% of the particles to depart vs. $\overline{m}$. Note the jump in T which occurs at the percolation threshold separating the localized regime from the diffusive regime.

In this work we studied the dynamics of particles which form multiple, reversible key-lock bridges. There is a *percolation transition* which separates the regime in which particles are localized near their original location from the regime where they exhibit diffusive behavior by breaking and reforming bridges. At low coverage the key-locking system exhibits a broad, power law like distribution of departure times, but no lateral diffusion. Above the percolation transition ($\overline{m} = \log 2$) diffusion allows the particle to cascade into deeper energy wells with a large number of key-lock bridges. This leads to an increase in the bound state lifetime similar to *aging* in glassy systems. The statistics for the particles' in-plane diffusion were determined. For relatively weak key-lock interactions there is a finite renormalization of the diffusion coefficient. However, as Δ increases, the system exhibits anomalous, sub-diffusive behavior analogous to dispersive transport in disordered semiconductors. We discussed the connection between our work and recent experiments with DNA-coated colloids. The findings indicate that the optimal regime for colloidal crystallization, where particle departure is a relatively fast process, is to have a large number of weakly bound key-lock bridges.

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